REMARKS

The following remarks are in response to the Office Action dated May 14, 2007 (the "Office Action") and the Advisory Action dated September 27, 2007 (the "Advisory Action"). Applicants have amended claims 1, 13-17, 23, 32, 37, 39, 52, and 53. Applicants have amended claims 1, 15-17, 23, and 52 to recite methods for immunizing a vertebrate or mammal with a composition consisting essentially of a set of plasmids (or two or more sets of plasmids) in a physiologically acceptable medium. Applicants have amended claim 32 to require that the plasmids be administered with a gene gun. These amendments are supported by the specification as filed, e.g., in the original claims, and in the Examples. Claims 15 and 23 have also been amended to be in independent form. Claim 16 has been amended to recite "two" or more sets of plasmid vectors rather than "one" or more sets of plasmid vectors. Dependent claims have been amended to use claim language consistent with the independent claims. No new matter has been added.

Applicants acknowledge the withdrawal of the rejection of claims 1-56 as lacking enablement.

The amendments and remarks herein concerning the rejections under 35 U.S.C. §§ 102 and 112, second paragraph, and on the grounds of obviousness-type double patenting, are identical to the amendment and remarks in the reply filed September 14, 2007. In addition, Applicants note the following in response to remarks in the Advisory Action. According to the Advisory Action, the amendment to claim 1 "introduces new limitations necessitating additional art rejections, regarding administering 'a set of plasmid vectors.'" The amendment to the claims to refer to a "set" or "sets" of plasmids is for clarity and does not alter the scope of the claims originally examined. The Advisory Action also stated that claim 32 "introduces new limitations necessitating additional art rejections, regarding the use of a gene gun." The scope of the claims originally examined encompassed administration with a gene gun.

Rejections under 35 U.S.C. § 102

Dyall-Smith et al., U.S. Pat. 5,332,658

Claims 1-2, 4, 8, 11-12, 14, 16, 17, 19, 27, and 30-31 were rejected as allegedly anticipated by Dyall-Smith et al. (U.S. Pat. 5,332,658; "the '658 patent").[1]

The Office Action states:

> Dyall-Smith et al. do indeed teach immunizing a vertebrate with a plasmid comprising a rotavirus antigen. Dyall-Smith et al. teach 'the isolated gene encoding all or part of the VP7 protein of human [rotavirus] serotype 4...inserted into an appropriate vector, such as a bacterial plasmid...for expression of the corresponding polypeptide in host cells' (col. 2, lines 12-15)...Dyall-Smith et al. go on to teach 'suitable microorganism expressing the major protein of human rotavirus serotype 4...on the cell surface will, on administration, enter the intestine, invade the lining of the guy...causing the production of protective antibodies in situ' (col. 2, lines 62-68). Therefore, the method of Dyall-Smith et al. clearly anticipates a plasmid-based vaccination against rotavirus, as claimed in the instant claims (pages 5-6).

This rejection is respectfully traversed. Claims 1, 16, 17, and their dependent claims, as amended, are directed to methods of immunizing a vertebrate by administering a composition consisting essentially of a set of plasmid vectors (or two or more sets of plasmid vectors) in a physiologically acceptable medium, whereby a humoral immune response, cell mediated immune response, or both a humoral and cell mediated response, are elicited.

The '658 patent does not disclose plasmid-based vaccination. The cited passage at col. 2, lines 12-15, of the '658 patent discloses that a VP7 gene or portion thereof "may be inserted into an appropriate expression vector, such as a bacterial plasmid, SV40, adenovirus or phage DNA, for expression of the corresponding polypeptide in host cells (including bacterial or yeast and other eukaryotic host cells) containing these vectors or derivatives thereof." This is not a teaching to use a plasmid for immunization. It merely says that one may place a VP7 gene or portion into an expression vector. One of skill in the art would understand that the reference to "host cells" in this context refers to a "host" to the plasmid itself. Bacterial or yeast cells, which are disclosed as suitable "host cells," are not natural hosts to animal viruses, but can be used to express a protein of the animal virus. Subsequent passages at col. 2, lines 16-42, of the '658

[1] In the Office Action, the prior rejection of claims 1, 4, 8, 14, 16, 17, 27, 30, and 31 as allegedly anticipated by the '658 patent is maintained at pages 5-6. A separate rejection of claims 1-2, 4, 8, 11-12, 14, 16, 17, 19, 27, and 30-31 over the same reference is set forth at pages 9-11 of the Office Action. These rejections are discussed together here.

patent discuss such methods for expression of recombinant VP7 polypeptides, but do not direct one to practice immunization with a composition consisting essentially of a set of plasmids.

The '658 patent discusses vaccination with "the **polypeptides** encoded by the gene, or a portion or subunit thereof" (col. 2, lines 43-44; emphasis added). The patent then describes vaccine production of such polypeptides in host bacteria or yeast cells (col. 2, lines 47-53). It also refers to use of microorganisms transfected with a vector that expresses the gene as vaccines (col. 2, lines 54-67). Next, the patent describes vaccines that include viral vectors such as adenovirus or vaccinia (col. 3, lines 1-9). The vaccines described by the '658 patent require polypeptides or microorganisms such as bacteria or viruses. These polypeptide compositions are not the same as the plasmid vectors recited in the claimed methods. In addition, a microorganism composition (e.g., containing bacterial cells or virus particles) includes non-nucleic acid components associated with the microorganism, such as membrane components and polypeptides, and does not "consist essentially of" a set of plasmid vectors and a physiologically acceptable medium. Thus, the '658 patent does not disclose or suggest any of the presently claimed methods. Applicants respectfully request withdrawal of the rejection of the claims as allegedly anticipated by this reference.

Eppstein et al., U.S. Pat. 5,049,386

The rejection of claims 1-4, 6, 11-23, 25, and 30-35, as allegedly anticipated by Eppstein et al. (U.S. Pat. 5,049,386; "the '386 patent"), was maintained. According to the Office Action (page 7):

> Eppstein et al. do suggest a DNA vaccine. Clearly, Eppstein et al. teach liposome compositions comprising 'plasmids containing...sequences to yield the corresponding expressed products (e.g., proteins and peptides)' and 'intracellular delivery...in the whole organism' (col. 10, lines 27, 32-33, 43-44).

Applicants respectfully traverse this rejection and disagree that the '386 patent directs one to use DNA-containing compositions for immunization to induce immune responses. The '386 patent's generic disclosure to use compounds of Formula I to achieve "desirable intracellular delivery of specific biologically active substances, such as nucleosides, nucleotides, oligo- and poly-nucleotides, steroids, peptides, and proteins, and other appropriate natural or

synthetic molecules or macromolecules" (col. 10, lines 14-19) is not a suggestion to immunize with plasmid vectors. The '386 patent discusses vaccination in the context of immunization with "antigens."

The Office cited Eppstein's definition at col. 6, lines 30-31, that "an antigen is any substance to which an organism can elicit an immune response" as evidence that "plasmid DNA could be encompassed by this definition" (Office Action, page 7). Applicants disagree that this broad definition has anything at all to do with methods of immunizing vertebrates using a composition consisting essentially of a set of plasmid vectors, or with a method of administering plasmids using a gene gun.

The specification of the present application teaches that "uptake of DNA transcription units by host cells results in the expression of the desired antigen or antigens, thereby eliciting humoral or cell-mediated immune responses or both humoral and cell-mediated immune responses" (specification, page 2, lines 17-21). The claims employ compositions consisting essentially of a set of plasmid vectors, or methods of administering plasmids using a gene gun. Plasmid DNA is not administered as an antigen *per se*, to elicit an immune response against the DNA itself. Rather, it is administered to cause expression in the animal of a polypeptide that elicits an immune response. The '386 patent does not anywhere suggest using plasmids in this manner.

Moreover, the standard for anticipation is not whether the reference "is suggesting that" a claim limitation "could be encompassed" by a definition in the reference as recited at page 7, lines 8-9, of the Action. Nor is the standard whether a cited reference has "no contrary teaching" against a claimed method as recited at page 7, lines 16-17, of the Action. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131. A teaching to immunize with a plasmid composition is lacking in the '386 patent, not to mention a teaching to immunize according to methods that meet all of the elements of applicants' claims.

Furthermore, all of the methods disclosed by the '386 patent require use of a lipophilic composition. For example, where the '386 patent discusses peptide-based vaccines, it states that "to achieve the desired immune response, the antigen in the formulation comprising a compound of Formula I is administered to an animal or mammal in need thereof" (col. 15, lines 7-10).

Compounds of Formula I require a specific chemical structure and are "positively charged liposome forming lipids, which can be used for the formulation of positively charged liposomes in which drugs or other materials can be encapsulated in the conventional manner" (col. 4, lines 62-67). In the present case, the methods of claims 1, 16, 17, 32, and dependent claims, refer to compositions that consist essentially of a plasmid vector in a physiologically acceptable medium, or compositions administered with a gene gun. These methods do not employ the lipophilic compositions described in the '386 patent. The '386 patent does not suggest any uses of plasmids without lipophilic compositions. In view of the foregoing, applicants respectfully request withdrawal of the rejection.

Pistor et al., Klin. Wochenschr, 66:110-116, 1988

Claims 1-4, 6, 7, 11, 12, 14, 16-19, 25, 26, 30, 31, and 52-56 were rejected as allegedly anticipated by Pistor et al. (Klin. Wochenschr., 66:110-116, 1988 ; "Pistor"). The Office Action stated (page 12):

> Pistor et al teach 'expression of foreign protein molecule on the *E. coli* bacterial surface has been achieved through hybrid plasmid construction of fusion proteins using outer membrane protein ompA as a carrier system' (abstract)...Pistor et al. also teach 'Expression of foreign protein molecules on bacterial outer membranes according to the procedure presented here appears to have the potential of a convenient antigen-presentation technique...antigen presentation on bacterial surfaces might be useful for vaccination purposes, e.g., for enteric viral antigens.' (page 115, Discussion, parag. 2).

Applicants respectfully traverse this rejection. Pistor does not disclose methods of immunizing vertebrates using a composition consisting essentially of a set of plasmid vectors in a physiologically acceptable medium, or with a gene gun. Pistor's suggestion that "antigen presentation on bacterial surfaces might be useful for vaccination purposes" at page 115 requires administration of bacteria that display polypeptides. This vaccination concept is different than that of the present claims, which do not employ administration of bacterial cells. Applicants respectfully request withdrawal of this rejection.

Obviousness-Type Double Patenting

Claims 1-4, 6, 7, 11-14, 16-22, 25, 26, 30, 31, and 52-56 were rejected under the doctrine of obviousness-type double patenting as unpatentable over claims 1-19 of U.S. Pat. No. 5,643,578. Applicants provided appropriate terminal disclaimers with the Amendment filed September 14, 2007. Accordingly, this rejection should be overcome.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 37-39 were rejected as indefinite for depending from rejected claim 36. This rejection is overcome by the present amendment to claims 37 and 39 to depend from claim 32. Withdrawal of this rejection is requested.

CONCLUSION

Applicants submit that the claims are in condition for allowance and such action is requested. A Petition for Extension of Time and required fees are being filed herewith. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07917-217002.

Respectfully submitted,

Date: October 31, 2007

for Margo Fuma Reg. No. 59,812
J. Peter Fasse
Reg. No. 32,983

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906